

ATTACHMENT C.2

INDUCTION STUDY: DATA TABLES

Table 1: CYP1A2 Activity in Cryopreserved Human Hepatocytes Following Incubation with 50 µM Omeprazole

Sample Identification	Acetaminophen formation			Specific Activity		Percent of VC
	Raw (µM)	Adjusted (µM)		(pmol/min/million cells)	Individual	
Donor 1						
VC	0.05388	0.0539	0.0487 ± 0.00543	0.481	0.435 ± 0.0485	100
	0.05227	0.0523		0.467		
	0.04658	0.0466		0.416		
	0.04203	0.0420		0.375		
50 µM Omeprazole	0.95167	0.952	0.987 ± 0.0697	8.50	8.81 ± 0.623	2,027
	1.07407	1.07		9.59		
	0.91389	0.914		8.16		
	1.00737	1.01		8.99		
Donor 2						
VC	0.03023	0.0302	0.0300 ± 0.00305	0.270	0.267 ± 0.0272	100
	0.03210	0.0321		0.287		
	0.03193	0.0319		0.285		
	0.02556	0.0256		0.228		
50 µM Omeprazole	0.31279	0.313	0.256 ± 0.0475	2.79	2.28 ± 0.424	854
	0.21399	0.214		1.91		
	0.27687	0.277		2.47		
	0.21933	0.219		1.96		
Donor 3						
VC	0.04357	0.0436	0.0410 ± 0.00447	0.389	0.366 ± 0.0399	100
	0.04576	0.0458		0.409		
	0.03607	0.0361		0.322		
	0.03849	0.0385		0.344		
50 µM Omeprazole	1.21524	1.215	0.932 ± 0.192	10.9	8.33 ± 1.72	2,276
	0.78444	0.784		7.00		
	0.87427	0.874		7.81		
	0.85595	0.856		7.64		

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 2: CYP3A4 Activity in Cryopreserved Human Hepatocytes Following Incubation with 25 µM Rifampin

Sample Identification	6β-Hydroxytestosterone formation			Specific Activity		Percent of VC	
	Raw (µM)	Adjusted (µM)		(pmol/min/million cells)	Individual Mean ± SD		
		Individual	Mean ± SD				
Donor 1							
VC	0.05693 *	<0.100	<0.100 ± 0.000	<0.893	<0.893 ± 0.000	100	
Rifampin	1.22302	1.22	1.15 ± 0.109	10.9	10.3 ± 0.972	>1,153	
	0.05726 *	<0.100		<0.893			
	0.05367 *	<0.100		<0.893			
	0.04590 *	<0.100		<0.893			
25 µM	1.23746	1.24		11.0			
Rifampin	1.14988	1.15		10.3			
	0.99967	1.00		8.93			
Donor 2							
VC	0.12401	0.124	<0.117 ± 0.0141	1.11	<1.05 ± 0.126	100	
Rifampin	0.13222	0.132		1.18			
	0.07973 *	<0.100		<0.893			
	0.11219	0.112		1.00			
25 µM	0.90574	0.906	0.898 ± 0.120	8.09	8.01 ± 1.08	>766	
Rifampin	1.05531	1.06		9.42			
	0.86362	0.864		7.71			
	0.76548	0.765		6.83			
Donor 3							
VC	0.06064 *	<0.100	<0.100 ± 0.000	<0.893	<0.893 ± 0.000	100	
Rifampin	1.41954	1.42	1.51 ± 0.220	12.7	13.5 ± 1.97	>1,511	
	0.05981 *	<0.100		<0.893			
	0.06402 *	<0.100		<0.893			
	0.08660 *	<0.100		<0.893			
25 µM	1.83715	1.84		16.4			
Rifampin	1.43319	1.43		12.8			
	1.35405	1.35		12.1			

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

* The observed analyzed value (µM) was below the lowest concentration on the standard curve (0.1 µM).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 3: CYP1A2 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	Acetaminophen formation			Specific Activity (pmol/min/million cells)		Percent of VC
	Raw (μ M)	Individual	Adjusted (μ M)	Individual	Mean \pm SD	
Donor 1						
0 (VC)	0.05388	0.0539	0.0487 \pm 0.00543	0.481	0.435 \pm 0.0485	100
	0.05227	0.0523		0.467		
	0.04658	0.0466		0.416		
	0.04203	0.0420		0.375		
0.4	0.05121	0.0512	0.0537 \pm 0.00309	0.457	0.479 \pm 0.0276	110
	0.05264	0.0526		0.470		
	0.05714	0.0571		0.510		
4	0.07410	0.0741	0.0638 \pm 0.0193	0.662	0.570 \pm 0.172	131
	0.07581	0.0758		0.677		
	0.04160	0.0416		0.371		
40	0.15156	0.152	0.161 \pm 0.0133	1.35	1.44 \pm 0.119	332
	0.15617	0.156		1.39		
	0.17659	0.177		1.58		
Donor 2						
0 (VC)	0.03023	0.0302	0.0300 \pm 0.00305	0.270	0.267 \pm 0.0272	100
	0.03210	0.0321		0.287		
	0.03193	0.0319		0.285		
	0.02556	0.0256		0.228		
0.4	0.03165	0.0317	0.0323 \pm 0.000850	0.283	0.289 \pm 0.00759	108
	0.03208	0.0321		0.286		
	0.03329	0.0333		0.297		
4	0.03346	0.0335	0.0340 \pm 0.00198	0.299	0.304 \pm 0.0177	113
	0.03619	0.0362		0.323		
	0.03234	0.0323		0.289		
40	0.06015	0.0602	0.0589 \pm 0.00795	0.537	0.526 \pm 0.0710	197
	0.06616	0.0662		0.591		
	0.05040	0.0504		0.450		
Donor 3						
0 (VC)	0.04357	0.0436	0.0410 \pm 0.00447	0.389	0.366 \pm 0.0399	100
	0.04576	0.0458		0.409		
	0.03607	0.0361		0.322		
	0.03849	0.0385		0.344		
0.4	0.04030	0.0403	0.0438 \pm 0.00361	0.360	0.391 \pm 0.0322	107
	0.04347	0.0435		0.388		
	0.04750	0.0475		0.424		
4	0.04411	0.0441	0.0443 \pm 0.000214	0.394	0.396 \pm 0.00191	108
	0.04453	0.0445		0.398		
	0.04425	0.0443		0.395		
40	0.12276	0.123	0.122 \pm 0.00365	1.10	1.09 \pm 0.0326	297
	0.11776	0.118		1.05		
	0.12487	0.125		1.11		

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 4a: CYP2A6 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	Raw (μ M)	Metabolite formation		Specific Activity (pmol/min/million cells)		Percent of VC
		Individual	Adjusted (μ M) Mean \pm SD	Individual	Mean \pm SD	
7-Hydroxycoumarin (7-HC) Formation: Donor 1						
0 (VC)	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
0.4	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
4	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
40	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
7-Hydroxycoumarin (7-HC) Formation: Donor 2						
0 (VC)	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
0.4	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
4	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
40	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
7-Hydroxycoumarin (7-HC) Formation: Donor 3						
0 (VC)	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
0.4	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
4	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		
40	0.00000 *	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.00000 *	<0.100		<0.893		
	0.00000 *	<0.100		<0.893		

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

* The observed analyzed value (μ M) was below the lowest concentration on the standard curve (0.1 μ M).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 4b: CYP2A6 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	Metabolite formation			Specific Activity (pmol/min/million cells)		Percent of VC
	Raw (μ M)	Adjusted (μ M)	Individual Mean \pm SD	Individual	Mean \pm SD	
7-Hydroxycoumarin Glucuronide (7-HCG) Formation: Donor 1						
0 (VC)	0.01705 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00000 ^b	<0.0500		<0.446		
	0.00000 ^b	<0.0500		<0.446		
	0.00000 ^b	<0.0500		<0.446		
0.4	0.00000 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00000 ^b	<0.0500		<0.446		
	0.00000 ^b	<0.0500		<0.446		
4	0.00000 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00000 ^b	<0.0500		<0.446		
	0.00000 ^b	<0.0500		<0.446		
40	0.00000 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00000 ^b	<0.0500		<0.446		
	0.00000 ^b	<0.0500		<0.446		
7-Hydroxycoumarin Glucuronide (7-HCG) Formation: Donor 2						
0 (VC)	0.03808 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.04134 ^b	<0.0500		<0.446		
	0.03654 ^b	<0.0500		<0.446		
	0.03196 ^b	<0.0500		<0.446		
0.4	0.02245 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.03808 ^b	<0.0500		<0.446		
	0.03808 ^b	<0.0500		<0.446		
4	0.03437 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.03526 ^b	<0.0500		<0.446		
	0.02966 ^b	<0.0500		<0.446		
40	0.02926 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.02664 ^b	<0.0500		<0.446		
	0.03334 ^b	<0.0500		<0.446		
7-Hydroxycoumarin Glucuronide (7-HCG) Formation: Donor 3						
0 (VC)	0.00000 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.01964 ^b	<0.0500		<0.446		
	0.02373 ^b	<0.0500		<0.446		
	0.00000 ^b	<0.0500		<0.446		
0.4	0.02156 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.01820 ^b	<0.0500		<0.446		
	0.01816 ^b	<0.0500		<0.446		
4	0.00000 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.01965 ^b	<0.0500		<0.446		
	0.01624 ^b	<0.0500		<0.446		
40	0.00000 ^b	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.01883 ^b	<0.0500		<0.446		
	0.00000 ^b	<0.0500		<0.446		

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

^bThe observed analyzed value (μ M) was below the lowest concentration on the standard curve (0.05 μ M).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 4c: CYP2A6 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	Metabolite formation			Specific Activity (pmol/min/million cells)		Percent of VC
	Raw (μ M)	Individual	Adjusted (μ M) Mean \pm SD	Individual	Mean \pm SD	
7-Hydroxycoumarin Sulfate (7-HCS) Formation: Donor 1						
0 (VC)	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
0.4	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
4	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
40	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
7-Hydroxycoumarin Sulfate (7-HCS) Formation: Donor 2						
0 (VC)	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
0.4	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
4	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
40	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
7-Hydroxycoumarin Sulfate (7-HCS) Formation: Donor 3						
0 (VC)	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
0.4	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
4	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		
40	0.00000 °	<0.150	<0.150 \pm 0.000	<1.34	<1.34 \pm 0.000	100
	0.00000 °	<0.150		<1.34		
	0.00000 °	<0.150		<1.34		

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

° The observed analyzed value (μ M) was below the lowest concentration on the standard curve (0.15 μ M).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 4d: CYP2A6 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	Raw (μ M)	Metabolite formation		Specific Activity		Percent of VC
		Adjusted (μ M)		Individual	Mean \pm SD	
		Individual	Mean \pm SD	Individual	Mean \pm SD	
Total Metabolite Formation: Donor 1						
0 (VC)	0.0171 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.000 ^d	<0.300		<2.68		
	0.000 ^d	<0.300		<2.68		
	0.000 ^d	<0.300		<2.68		
0.4	0.000 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.000 ^d	<0.300		<2.68		
	0.000 ^d	<0.300		<2.68		
4	0.000 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.000 ^d	<0.300		<2.68		
	0.000 ^d	<0.300		<2.68		
40	0.000 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.000 ^d	<0.300		<2.68		
	0.000 ^d	<0.300		<2.68		
Total Metabolite Formation: Donor 2						
0 (VC)	0.0381 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.0413 ^d	<0.300		<2.68		
	0.0365 ^d	<0.300		<2.68		
	0.0320 ^d	<0.300		<2.68		
0.4	0.0225 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.0381 ^d	<0.300		<2.68		
	0.0381 ^d	<0.300		<2.68		
4	0.0344 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.0353 ^d	<0.300		<2.68		
	0.0297 ^d	<0.300		<2.68		
40	0.0293 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.0266 ^d	<0.300		<2.68		
	0.0333 ^d	<0.300		<2.68		
Total Metabolite Formation: Donor 3						
0 (VC)	0.000 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.0196 ^d	<0.300		<2.68		
	0.0237 ^d	<0.300		<2.68		
	0.000 ^d	<0.300		<2.68		
0.4	0.0216 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.0182 ^d	<0.300		<2.68		
	0.0182 ^d	<0.300		<2.68		
4	0.000 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.0197 ^d	<0.300		<2.68		
	0.0162 ^d	<0.300		<2.68		
40	0.000 ^d	<0.300	<0.300 \pm 0.000	<2.68	<2.68 \pm 0.000	100
	0.0188 ^d	<0.300		<2.68		
	0.000 ^d	<0.300		<2.68		

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

^dThe observed analyzed value (μ M) for all metabolites were below the lowest concentration on the corresponding standard curve.

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 5a: CYP2B6 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	Nirvanol formation			Specific Activity (pmol/min/million cells)		Percent of VC	
	Raw (μ M)	Adjusted (μ M)		Individual	Mean \pm SD		
		Individual	Mean \pm SD				
Donor 1							
0 (VC)	0.03230	0.0323	0.0319 \pm 0.00156	0.288	0.285 \pm 0.0139	100	
	0.03384	0.0338		0.302			
	0.03014	0.0301		0.269			
	0.03141	0.0314		0.280			
0.4	0.03380	0.0338	0.0340 \pm 0.000883	0.302	0.304 \pm 0.00789	107	
	0.03329	0.0333		0.297			
	0.03501	0.0350		0.313			
4	0.02742	0.0274	0.0305 \pm 0.00272	0.245	0.273 \pm 0.0243	95.7	
	0.03241	0.0324		0.289			
	0.03178	0.0318		0.284			
40	0.03233	0.0323	0.0310 \pm 0.00204	0.289	0.277 \pm 0.0182	97.1	
	0.03203	0.0320		0.286			
	0.02866	0.0287		0.256			
Donor 2							
0 (VC)	0.02927	0.0293	0.0289 \pm 0.00230	0.261	0.258 \pm 0.0205	100	
	0.02920	0.0292		0.261			
	0.03137	0.0314		0.280			
	0.02582	0.0258		0.231			
0.4	0.02544	0.0254	0.0306 \pm 0.00559	0.227	0.273 \pm 0.0499	106	
	0.02986	0.0299		0.267			
	0.03654	0.0365		0.326			
4	0.02852	0.0285	0.0281 \pm 0.000884	0.255	0.250 \pm 0.00790	97.0	
	0.02703	0.0270		0.241			
	0.02860	0.0286		0.255			
40	0.00341 ^a	<0.0250	<0.0250 \pm 0.000	<0.223	<0.223 \pm 0.000	<86.5	
	0.00320 ^a	<0.0250		<0.223			
	0.00330 ^a	<0.0250		<0.223			
Donor 3							
0 (VC)	0.02349 ^a	<0.0250	<0.0252 \pm 0.000435	<0.223	<0.225 \pm 0.00388	100	
	0.02587	0.0259		0.231			
	0.02376 ^a	<0.0250		<0.223			
	0.02236 ^a	<0.0250		<0.223			
0.4	0.02177 ^a	<0.0250	<0.0250 \pm 0.000	<0.223	<0.223 \pm 0.000	99.1	
	0.02343 ^a	<0.0250		<0.223			
	0.02326 ^a	<0.0250		<0.223			
4	0.02392 ^a	<0.0250	<0.0250 \pm 0.000	<0.223	<0.223 \pm 0.000	99.1	
	0.02490 ^a	<0.0250		<0.223			
	0.02229 ^a	<0.0250		<0.223			
40	0.02005 ^a	<0.0250	<0.0250 \pm 0.000	<0.223	<0.223 \pm 0.000	99.1	
	0.01976 ^a	<0.0250		<0.223			
	0.02169 ^a	<0.0250		<0.223			

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

^aThe observed analyzed value (μ M) was below the lowest concentration on the standard curve (0.025 μ M).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 5b: CYP2B6 Activity in Cryopreserved Human Hepatocytes Following Incubation with 1 mM Phenobarbital

Sample Identification	Raw (µM)	Nirvanol formation		Specific Activity (pmol/min/million cells)		Percent of VC
		Adjusted (µM)		Individual	Mean ± SD	
		Individual	Mean ± SD	Individual	Mean ± SD	
Donor 1						
VC	0.03230	0.0323	0.0319 ± 0.00156	0.288	0.285 ± 0.0139	100
	0.03384	0.0338		0.302		
	0.03014	0.0301		0.269		
	0.03141	0.0314		0.280		
1 mM Phenobarbital	0.10875	0.109	0.107 ± 0.00957	0.971	0.955 ± 0.0854	335
	0.11143	0.111		0.995		
	0.11462	0.115		1.02		
	0.09308	0.0931		0.831		
Donor 2						
VC	0.02927	0.0293	0.0289 ± 0.00230	0.261	0.258 ± 0.0205	100
	0.02920	0.0292		0.261		
	0.03137	0.0314		0.280		
	0.02582	0.0258		0.231		
1 mM Phenobarbital	0.04920	0.0492	0.0461 ± 0.00398	0.439	0.411 ± 0.0355	159
	0.04148	0.0415		0.370		
	0.04957	0.0496		0.443		
	0.04398	0.0440		0.393		
Donor 3						
VC	0.02349 *	<0.0250	<0.0252 ± 0.000435	<0.223	<0.225 ± 0.00388	100
	0.02587	0.0259		0.231		
	0.02376 *	<0.0250		<0.223		
	0.02236 *	<0.0250		<0.223		
1 mM Phenobarbital	0.08499	0.0850	0.0775 ± 0.00718	0.759	0.692 ± 0.0641	>307
	0.07505	0.0751		0.670		
	0.08123	0.0812		0.725		
	0.06864	0.0686		0.613		

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol).

* The observed analyzed value (µM) was below the lowest concentration on the standard curve (0.1 µM).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 6a: CYP2C8 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	6-Hydroxypaclitaxel formation			Specific Activity (pmol/min/million cells)		Percent of VC	
	Raw (μ M)	Adjusted (μ M)		Individual	Mean \pm SD		
		Individual	Mean \pm SD				
Donor 1							
0 (VC)	0.02260 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100	
	0.02001 *	<0.0500		<0.446			
	0.00000 *	<0.0500		<0.446			
	0.00000 *	<0.0500		<0.446			
0.4	0.04455 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100	
	0.00000 *	<0.0500		<0.446			
	0.00000 *	<0.0500		<0.446			
4	0.01755 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100	
	0.02331 *	<0.0500		<0.446			
	0.03323 *	<0.0500		<0.446			
40	0.02273 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100	
	0.01761 *	<0.0500		<0.446			
	0.03963 *	<0.0500		<0.446			
Donor 2							
0 (VC)	0.03939 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100	
	0.03720 *	<0.0500		<0.446			
	0.01756 *	<0.0500		<0.446			
	0.02379 *	<0.0500		<0.446			
0.4	0.25343	0.253	<0.177 \pm 0.111	2.26	<1.58 \pm 0.991	355	
	0.03299 *	<0.0500		<0.446			
	0.22856	0.229		2.04			
4	0.03716 *	<0.0500	<0.0561 \pm 0.0105	<0.446	<0.501 \pm 0.0939	112	
	0.02847 *	<0.0500		<0.446			
	0.06821	0.0682		0.609			
40	0.05953	0.0595	<0.0532 \pm 0.00550	0.532	<0.475 \pm 0.0491	106	
	0.03151 *	<0.0500		<0.446			
	0.01820 *	<0.0500		<0.446			
Donor 3							
0 (VC)	0.04414 *	<0.0500	<0.0549 \pm 0.00985	<0.446	<0.490 \pm 0.0879	100	
	0.03780 *	<0.0500		<0.446			
	0.06970	0.0697		0.622			
	0.01934 *	<0.0500		<0.446			
0.4	0.50538	0.505	<0.228 \pm 0.243	4.51	<2.04 \pm 2.17	415	
	0.03692 *	<0.0500		<0.446			
	0.12852	0.129		1.15			
4	0.03195 *	<0.0500	<0.0990 \pm 0.0542	<0.446	<0.884 \pm 0.484	180	
	0.15728	0.157		1.40			
	0.08980	0.0898		0.802			
40	0.49287	0.493	<0.198 \pm 0.256	4.40	<1.76 \pm 2.28	360	
	0.00000 *	<0.0500		<0.446			
	0.03062 *	<0.0500		<0.446			

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

* The observed analyzed value (μ M) was below the lowest concentration on the standard curve (0.05 μ M).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 6b: CYP2C8 Activity in Cryopreserved Human Hepatocytes Following Incubation with 25 µM Rifampin

Sample Identification	6-Hydroxypaclitaxel formation			Specific Activity		Percent of VC	
	Raw (µM)	Adjusted (µM)		(pmol/min/million cells)	Individual Mean ± SD		
		Individual	Mean ± SD				
Donor 1							
VC	0.02260 *	<0.0500	<0.0500 ± 0.000	<0.446	<0.446 ± 0.000	100	
	0.02001 *	<0.0500		<0.446			
	0.00000 *	<0.0500		<0.446			
	0.00000 *	<0.0500		<0.446			
25 µM Rifampin	0.01513 *	<0.0500	<0.0576 ± 0.0152	<0.446	<0.514 ± 0.135	115	
	0.02819 *	<0.0500		<0.446			
	0.08033 *	0.0803		0.717			
	0.00000 *	<0.0500		<0.446			
Donor 2							
VC	0.03939 *	<0.0500	<0.0500 ± 0.000	<0.446	<0.446 ± 0.000	100	
	0.03720 *	<0.0500		<0.446			
	0.01756 *	<0.0500		<0.446			
	0.02379 *	<0.0500		<0.446			
25 µM Rifampin	0.01592 *	<0.0500	<0.0681 ± 0.0361	<0.446	<0.608 ± 0.322	136	
	0.02262 *	<0.0500		<0.446			
	0.02859 *	<0.0500		<0.446			
	0.12220	0.122		1.09			
Donor 3							
VC	0.04414 *	<0.0500	<0.0549 ± 0.00985	<0.446	<0.490 ± 0.0879	100	
	0.03780 *	<0.0500		<0.446			
	0.06970	0.0697		0.622			
	0.01934 *	<0.0500		<0.446			
25 µM Rifampin	0.68053	0.681	<0.211 ± 0.313	6.08	<1.88 ± 2.80	384	
	0.06333	0.0633		0.565			
	0.03422 *	<0.0500		<0.446			
	0.01462 *	<0.0500		<0.446			

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

* The observed analyzed value (µM) was below the lowest concentration on the standard curve (0.05 µM).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 7a: CYP2C9 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	4'-Methylhydroxytolbutamide formation			Specific Activity (pmol/min/million cells)		Percent of VC	
	Raw (μ M)	Adjusted (μ M)		Individual	Mean \pm SD		
		Individual	Mean \pm SD				
Donor 1							
0 (VC)	0.01215	0.0122	0.0137 \pm 0.00161	0.108	0.122 \pm 0.0144	100	
	0.01502	0.0150		0.134			
	0.01513	0.0151		0.135			
	0.01245	0.0125		0.111			
0.4	0.01557	0.0156	0.0147 \pm 0.000753	0.139	0.132 \pm 0.00672	108	
	0.01410	0.0141		0.126			
	0.01455	0.0146		0.130			
4	0.01331	0.0133	0.0137 \pm 0.00136	0.119	0.122 \pm 0.0121	100	
	0.01523	0.0152		0.136			
	0.01261	0.0126		0.113			
40	0.00931 ^a	<0.0100	<0.0100 \pm 0.0000346	<0.0893	<0.0895 \pm 0.000309	<73.2	
	0.00952 ^a	<0.0100		<0.0893			
	0.01006	0.0101		0.0898			
Donor 2							
0 (VC)	0.05192	0.0519	0.0491 \pm 0.00479	0.464	0.438 \pm 0.0428	100	
	0.04864	0.0486		0.434			
	0.05325	0.0533		0.475			
	0.04250	0.0425		0.379			
0.4	0.04819	0.0482	0.0474 \pm 0.00223	0.430	0.423 \pm 0.0200	96.6	
	0.04489	0.0449		0.401			
	0.04915	0.0492		0.439			
4	0.04634	0.0463	0.0456 \pm 0.000864	0.414	0.407 \pm 0.00772	92.9	
	0.04581	0.0458		0.409			
	0.04465	0.0447		0.399			
40	0.02917	0.0292	0.0296 \pm 0.000651	0.260	0.265 \pm 0.00581	60.4	
	0.02936	0.0294		0.262			
	0.03038	0.0304		0.271			
Donor 3							
0 (VC)	0.02021	0.0202	0.0181 \pm 0.00206	0.180	0.162 \pm 0.0184	100	
	0.01700	0.0170		0.152			
	0.01952	0.0195		0.174			
	0.01586	0.0159		0.142			
0.4	0.02067	0.0207	0.0201 \pm 0.00125	0.185	0.179 \pm 0.0111	111	
	0.02096	0.0210		0.187			
	0.01867	0.0187		0.167			
4	0.01807	0.0181	0.0187 \pm 0.00235	0.161	0.167 \pm 0.0210	103	
	0.02129	0.0213		0.190			
	0.01671	0.0167		0.149			
40	0.01364	0.0136	0.0142 \pm 0.000560	0.122	0.127 \pm 0.00500	78.4	
	0.01432	0.0143		0.128			
	0.01475	0.0148		0.132			

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

^a The observed analyzed value (μ M) was below the lowest concentration on the standard curve (0.01 μ M).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 7b: CYP2C9 Activity in Cryopreserved Human Hepatocytes Following Incubation with 25 µM Rifampin

Sample Identification	4'-Methylhydroxytolbutamide formation			Specific Activity		Percent of VC
	Raw (µM)	Adjusted (µM)		(pmol/min/million cells)	Individual	
Donor 1						
VC	0.01215	0.0122	0.0137 ± 0.00161	0.108	0.122 ± 0.0144	100
	0.01502	0.0150		0.134		
	0.01513	0.0151		0.135		
	0.01245	0.0125		0.111		
25 µM Rifampin	0.02792	0.0279	0.0291 ± 0.00481	0.249	0.260 ± 0.0429	213
	0.03387	0.0339		0.302		
	0.03168	0.0317		0.283		
	0.02289	0.0229		0.204		
Donor 2						
VC	0.05192	0.0519	0.0491 ± 0.00479	0.464	0.438 ± 0.0428	100
	0.04864	0.0486		0.434		
	0.05325	0.0533		0.475		
	0.04250	0.0425		0.379		
25 µM Rifampin	0.05908	0.0591	0.0608 ± 0.00254	0.528	0.543 ± 0.0227	124
	0.06386	0.0639		0.570		
	0.06191	0.0619		0.553		
	0.05839	0.0584		0.521		
Donor 3						
VC	0.02021	0.0202	0.0181 ± 0.00206	0.180	0.162 ± 0.0184	100
	0.01700	0.0170		0.152		
	0.01952	0.0195		0.174		
	0.01586	0.0159		0.142		
25 µM Rifampin	0.03543	0.0354	0.0364 ± 0.00192	0.316	0.325 ± 0.0172	201
	0.03771	0.0377		0.337		
	0.03829	0.0383		0.342		
	0.03419	0.0342		0.305		

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

^a The observed analyzed value (µM) was below the lowest concentration on the standard curve (0.1 µM).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 8a: CYP2C19 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	4'-Hydroxymephenytoin formation			Specific Activity		Percent of VC
	Raw (μ M)	Individual	Adjusted (μ M) Mean \pm SD	Individual	(pmol/min/million cells) Mean \pm SD	
Donor 1						
0 (VC)	0.00025 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00058 *	<0.0500		<0.446		
	0.00114 *	<0.0500		<0.446		
	0.00058 *	<0.0500		<0.446		
0.4	0.00708 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.01319 *	<0.0500		<0.446		
	0.01861 *	<0.0500		<0.446		
4	0.01649 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00029 *	<0.0500		<0.446		
	0.00064 *	<0.0500		<0.446		
40	0.00057 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00031 *	<0.0500		<0.446		
	0.00037 *	<0.0500		<0.446		
Donor 2						
0 (VC)	N/A *	N/A	<0.0500 \pm 0.000	N/A	<0.446 \pm 0.000	100
	0.01146 *	<0.0500		<0.446		
	0.01456 *	<0.0500		<0.446		
	N/A *	N/A		N/A		
0.4	0.00765 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00779 *	<0.0500		<0.446		
	0.00808 *	<0.0500		<0.446		
4	0.00775 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00744 *	<0.0500		<0.446		
	0.00773 *	<0.0500		<0.446		
40	0.00697 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00840 *	<0.0500		<0.446		
	0.00790 *	<0.0500		<0.446		
Donor 3						
0 (VC)	0.00026 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00000 *	<0.0500		<0.446		
	0.00000 *	<0.0500		<0.446		
	0.00000 *	<0.0500		<0.446		
0.4	0.00000 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00000 *	<0.0500		<0.446		
	0.00023 *	<0.0500		<0.446		
4	0.00000 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00000 *	<0.0500		<0.446		
	0.00000 *	<0.0500		<0.446		
40	0.00191 *	<0.0500	<0.0500 \pm 0.000	<0.446	<0.446 \pm 0.000	100
	0.00000 *	<0.0500		<0.446		
	0.00000 *	<0.0500		<0.446		

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

* The observed analyzed value (μ M) was below the lowest concentration on the standard curve (0.05 μ M).

* Sample lost after preparation.

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 8b: CYP2C19 Activity in Cryopreserved Human Hepatocytes Following Incubation with 25 µM Rifampin

Sample Identification	4'-Hydroxymephenytoin formation			Specific Activity		Percent of VC	
	Raw (µM)	Adjusted (µM)		(pmol/min/million cells)	Individual Mean ± SD		
		Individual	Mean ± SD				
Donor 1							
VC	0.00025 *	<0.0500	<0.0500 ± 0.000	<0.446	<0.446 ± 0.000	100	
	0.00058 *	<0.0500		<0.446			
	0.00114 *	<0.0500		<0.446			
	0.00058 *	<0.0500		<0.446			
25 µM Rifampin	0.00708 *	<0.0500	<0.0500 ± 0.000	<0.446	<0.446 ± 0.000	100	
	0.01319 *	<0.0500		<0.446			
	0.01861 *	<0.0500		<0.446			
	0.01649 *	<0.0500		<0.446			
Donor 2							
VC	N/A *	N/A	<0.0500 ± 0.000	N/A	<0.446 ± 0.000	100	
	0.01146 *	<0.0500		<0.446			
	0.01456 *	<0.0500		<0.446			
	N/A *	N/A		N/A			
25 µM Rifampin	0.00986 *	<0.0500	<0.0500 ± 0.000	<0.446	<0.446 ± 0.000	100	
	0.01018 *	<0.0500		<0.446			
	0.01272 *	<0.0500		<0.446			
	0.00915 *	<0.0500		<0.446			
Donor 3							
VC	0.00026 *	<0.0500	<0.0500 ± 0.000	<0.446	<0.446 ± 0.000	100	
	0.00000 *	<0.0500		<0.446			
	0.00000 *	<0.0500		<0.446			
	0.00000 *	<0.0500		<0.446			
25 µM Rifampin	0.00142 *	<0.0500	<0.0500 ± 0.000	<0.446	<0.446 ± 0.000	100	
	0.00191 *	<0.0500		<0.446			
	0.00119 *	<0.0500		<0.446			
	0.00018 *	<0.0500		<0.446			

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

* The observed analyzed value (µM) was below the lowest concentration on the standard curve (0.05 µM).

* Samples were lost during analysis and therefore could not be analyzed.

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 9: CYP2D6 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	Dextrorphan formation			Specific Activity (pmol/min/million cells)		Percent of VC	
	Raw (μ M)	Adjusted (μ M)		Individual	Mean \pm SD		
		Individual	Mean \pm SD				
Donor 1							
0 (VC)	0.00772 ^a	<0.0100	<0.0100 \pm 0.000	<0.0893	<0.0893 \pm 0.000	100	
	0.00796 ^a	<0.0100		<0.0893			
	0.00736 ^a	<0.0100		<0.0893			
	0.00724 ^a	<0.0100		<0.0893			
0.4	0.00809 ^a	<0.0100	<0.0100 \pm 0.000	<0.0893	<0.0893 \pm 0.000	100	
	0.00749 ^a	<0.0100		<0.0893			
	0.00853 ^a	<0.0100		<0.0893			
4	0.00832 ^a	<0.0100	<0.0100 \pm 0.000	<0.0893	<0.0893 \pm 0.000	100	
	0.00721 ^a	<0.0100		<0.0893			
	0.00744 ^a	<0.0100		<0.0893			
40	0.00398 ^a	<0.0100	<0.0100 \pm 0.000	<0.0893	<0.0893 \pm 0.000	100	
	0.00205 ^a	<0.0100		<0.0893			
	0.00520 ^a	<0.0100		<0.0893			
Donor 2							
0 (VC)	0.01286	0.0129	0.0139 \pm 0.00152	0.115	0.124 \pm 0.0136	100	
	0.01432	0.0143		0.128			
	0.01581	0.0158		0.141			
	0.01247	0.0125		0.111			
0.4	0.01302	0.0130	0.0133 \pm 0.000485	0.116	0.119 \pm 0.00433	95.9	
	0.01302	0.0130		0.116			
	0.01386	0.0139		0.124			
4	0.01361	0.0136	0.0143 \pm 0.000589	0.122	0.128 \pm 0.00526	103	
	0.01468	0.0147		0.131			
	0.01457	0.0146		0.130			
40	0.00998 ^a	<0.0100	<0.0102 \pm 0.000260	<0.0893	<0.0906 \pm 0.00232	<73.2	
	0.00956 ^a	<0.0100		<0.0893			
	0.01045	0.0105		0.0933			
Donor 3							
0 (VC)	0.07011	0.0701	0.0665 \pm 0.00607	0.626	0.594 \pm 0.0542	100	
	0.05856	0.0586		0.523			
	0.07219	0.0722		0.645			
	0.06505	0.0651		0.581			
0.4	0.06218	0.0622	0.0657 \pm 0.00305	0.555	0.586 \pm 0.0272	98.8	
	0.06688	0.0669		0.597			
	0.06789	0.0679		0.606			
4	0.06071	0.0607	0.0597 \pm 0.00164	0.542	0.533 \pm 0.0146	89.8	
	0.06060	0.0606		0.541			
	0.05782	0.0578		0.516			
40	0.05087	0.0509	0.0489 \pm 0.00347	0.454	0.436 \pm 0.0310	73.5	
	0.05088	0.0509		0.454			
	0.04486	0.0449		0.401			

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

^aThe observed analyzed value (μ M) was below the lowest concentration on the standard curve (0.01 μ M).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 10: CYP2E1 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	6-Hydroxychlorzoxazone formation			Specific Activity (pmol/min/million cells)		Percent of VC	
	Raw (μ M)	Adjusted (μ M)		Individual	Mean \pm SD		
		Individual	Mean \pm SD				
Donor 1							
0 (VC)	0.28067	0.281	0.283 \pm 0.00460	2.51	2.53 \pm 0.0411	100	
	0.28793	0.288		2.57			
	0.28627	0.286		2.56			
	0.27817	0.278		2.48			
0.4	0.28854	0.289	0.277 \pm 0.0279	2.58	2.47 \pm 0.249	97.8	
	0.29749	0.297		2.66			
	0.24529	0.245		2.19			
4	0.28784	0.288	0.295 \pm 0.0236	2.57	2.64 \pm 0.210	104	
	0.27623	0.276		2.47			
	0.32160	0.322		2.87			
40	0.28453	0.285	0.294 \pm 0.00876	2.54	2.63 \pm 0.0782	104	
	0.29753	0.298		2.66			
	0.30121	0.301		2.69			
Donor 2							
0 (VC)	0.07385	0.0739	0.0748 \pm 0.00211	0.659	0.668 \pm 0.0188	100	
	0.07610	0.0761		0.679			
	0.07690	0.0769		0.687			
	0.07229	0.0723		0.645			
0.4	0.07071	0.0707	0.0776 \pm 0.00753	0.631	0.693 \pm 0.0673	104	
	0.07649	0.0765		0.683			
	0.08565	0.0857		0.765			
4	0.06315	0.0632	0.0670 \pm 0.00355	0.564	0.598 \pm 0.0317	89.6	
	0.06775	0.0678		0.605			
	0.07013	0.0701		0.626			
40	0.06247	0.0625	0.0745 \pm 0.0141	0.558	0.665 \pm 0.126	99.6	
	0.07091	0.0709		0.633			
	0.09003	0.0900		0.804			
Donor 3							
0 (VC)	0.05899	0.0590	0.0570 \pm 0.00420	0.527	0.509 \pm 0.0375	100	
	0.06077	0.0608		0.543			
	0.05718	0.0572		0.511			
	0.05110	0.0511		0.456			
0.4	0.05031	0.0503	0.0517 \pm 0.00140	0.449	0.462 \pm 0.0125	90.7	
	0.05310	0.0531		0.474			
	0.05169	0.0517		0.462			
4	0.05245	0.0525	0.0500 \pm 0.00389	0.468	0.446 \pm 0.0348	87.7	
	0.05202	0.0520		0.464			
	0.04550	0.0455		0.406			
40	0.05260	0.0526	0.0535 \pm 0.00164	0.470	0.478 \pm 0.0146	93.9	
	0.05541	0.0554		0.495			
	0.05254	0.0525		0.469			

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.

Table 11: CYP3A4 Activity in Cryopreserved Human Hepatocytes Following Incubation with Metaxalone

Metaxalone (μ M)	6 β -Hydroxytestosterone formation			Specific Activity		Percent of VC
	Raw (μ M)	Individual	Adjusted (μ M) Mean \pm SD	Individual	(pmol/min/million cells) Mean \pm SD	
Donor 1						
0 (VC)	0.05693 ^a	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.05726 ^a	<0.100		<0.893		
	0.05367 ^a	<0.100		<0.893		
	0.04590 ^a	<0.100		<0.893		
0.4	0.05415 ^a	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.06053 ^a	<0.100		<0.893		
	0.05911 ^a	<0.100		<0.893		
4	0.05783 ^a	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.05948 ^a	<0.100		<0.893		
	0.05705 ^a	<0.100		<0.893		
40	0.06888 ^a	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.06424 ^a	<0.100		<0.893		
	0.06511 ^a	<0.100		<0.893		
Donor 2						
0 (VC)	0.12401	0.124	<0.117 \pm 0.0141	1.11	<1.05 \pm 0.126	100
	0.13222	0.132		1.18		
	0.07973 ^a	<0.100		<0.893		
	0.11219	0.112		1.00		
0.4	0.12083	0.121	0.134 \pm 0.0122	1.08	1.20 \pm 0.109	>115
	0.14424	0.144		1.29		
	0.13828	0.138		1.23		
4	0.10953	0.110	0.116 \pm 0.00524	0.978	1.03 \pm 0.0468	>98.7
	0.11883	0.119		1.06		
	0.11837	0.118		1.06		
40	0.14198	0.142	0.141 \pm 0.00273	1.27	1.26 \pm 0.0244	>121
	0.14356	0.144		1.28		
	0.13824	0.138		1.23		
Donor 3						
0 (VC)	0.06064 ^a	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.05981 ^a	<0.100		<0.893		
	0.06402 ^a	<0.100		<0.893		
	0.08660 ^a	<0.100		<0.893		
0.4	0.05106 ^a	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.08255 ^a	<0.100		<0.893		
	0.05998 ^a	<0.100		<0.893		
4	0.06298 ^a	<0.100	<0.100 \pm 0.000	<0.893	<0.893 \pm 0.000	100
	0.05381 ^a	<0.100		<0.893		
	0.07264 ^a	<0.100		<0.893		
40	0.05587 ^a	<0.100	<0.101 \pm 0.00238	<0.893	<0.905 \pm 0.0213	101
	0.10413	0.104		0.930		
	0.08088 ^a	<0.100		<0.893		

Abbreviations: SD, standard deviation; VC, vehicle control (1% Methanol)

^aThe observed analyzed value (μ M) was below the lowest concentration on the standard curve (0.1 μ M).

Note: For all calculations above, the resulting values are shown with at least three significant figures for display purposes only.